A medical predictive system for comparative analysis of fetal parameters

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Abstract

A medical predictive system for comparative analysis of fetal parameters was motivated by the high rate of fetal loss in Nigeria which mostly occurs as a result of wrong medical predictive system. To solve this problem, software that will identify the fetal parameters that predicts the gestational age was developed. The new model will be a hybrid model. It will combine the Nagele's Rule and Mittendorf Rule to predict the fetal parameter. The new model will take the average of the two models as the predicted date of delivery. In this new system, it is noteworthy to name some ways of determining gestational age based on Last Menstrual Period (LMP). Therefore the proposed model will be a combination of the two model taking average of the number of days to be added to the LMP. This will be used to determine the Expected Date of Delivery in the new system designed. A platform for solving complication problems due to low and excessive birth weights at delivery by accurately estimating fetal parameters (Fetal Weight, Fetal Age, Conception Date, and Delivery Date) was implemented. This was implemented using externally generated data by combining the independent information about fetal size obtained from the three different approaches (i.e. clinical examination, quantitative assessment of maternal characteristics, ultrasonographic fetal biometry). Expert system methodology and Object Oriented Analysis and Design Methodology (OOADM) were adopted in the design of the predictive system. The new system allows the patients to access their antenatal visit records from any internet access point and the software developed helps physicians to accurately estimate the gestational age of the fetus and hence provide a support tool for estimating Gestation Age and to establish accuracy indicators that will provide tolerances for its later use in growth and health evaluation.

Keywords: Predictive system; ultrasonographic; Last Menstrual Period; Mittendorf Rule; Nagele’s Rule; Fetal parameter

1. Introduction

To improve the health care system for expectant mothers, accurate determination of gestational age (GA) is essential for the provision of appropriate obstetric and neonatal care, including treatment of infections during pregnancy with drugs that may be contraindicated in the first trimester, detection of growth restriction and post term pregnancies (42 weeks gestation), provision of antenatal corticosteroids during preterm labour, and decisions regarding whether to administer or withhold intensive care to extremely premature infants (Rijken, 2012). Fetal crown-rump length (CRL) measured by ultrasound between 7+0 and 13+6 weeks gestation is the recommended method for precise dating of spontaneously conceived pregnancies (Butt, 2014). Beyond 14 weeks, ultrasound up to 24 weeks is the upper recommended limit for accurate dating using other fetal biometry measurements including head circumference (HC) and biparietal diameter (BPD) (Mehta, 2012). However, in resource-limited settings GA assessment is prone to inaccuracy. While several publications have demonstrated successful sonography in resource-limited settings, quality routine ultrasound is rarely available (Wylie, 2013). Where ultrasound is available, late attendees to antenatal care or
Birth centres present dating issues in all settings because ultrasound biometry is less accurate and less precise when measured later during pregnancy (Haddrell, 2014). Therefore, estimating gestational age in the absence of CRL biometry is a problem of global significance.

Prior to ultrasound, various alternative methods were used to estimate GA. These methods are still widely practiced in resource-limited settings where ultrasound is unavailable, and in late presenters. Symphysis-pubis fundal height (SFH) measurements are commonly taken during antenatal care, and are used as a simple and inexpensive method of estimating GA from SFH growth charts (Sola, 1999); a formula for estimating GA from at least three SFH measurements specific to this study population has been developed and is accurate to ±2 weeks (White, 2012). Additionally, several clinical methods (requiring some technical expertise but little equipment or expenditure), such as the Ballard or the Dubowitz methods of GA assessment utilize external and neurological criteria of the newborn to determine GA at birth (Ballard, 1991). GA is also commonly calculated from the first day of the last menstrual period (LMP), but LMP is less well recalled in late attendees (Tunon, 1996), and determination of LMP can be impeded by low literacy rates and cultural factors (Rijken, 2012).

Accurate GA assessment is of particular significance in malaria endemic areas as the adverse maternal and fetal effects of exposure to malaria or anti-malarial drugs used for treatment may be modified by gestation (White, 2008). Additionally, although all methods of estimating GA will have a margin of error, large and systematic measurement error will lead to misclassification of adverse birth outcomes such as preterm birth, small for gestational age, intrauterine growth restriction, spontaneous abortion and stillbirth; misclassification will bias associations between exposure to malaria and anti-malarial drugs during pregnancy and adverse birth outcomes.

Hundreds of millions of pregnancies occur in resource-limited settings every year, including 125 million pregnancies at risk of malaria, where reliance on less accurate dating methods is common (Dellicour, 2010). Therefore, determining the relative accuracy of alternative methods for estimating GA is vitally important to inform clinical judgments in obstetric and neonatal care and in epidemiological research of malaria in pregnancy.

At present, clinical observation of these adaptations strongly relies on ultrasonography, a screening tool that makes it possible the biophysical assessment of fetal well-being and thus, the classification of pregnancy as in low-risk or high-risk status. Unfortunately, even though this technological option has been used since the end of the 60s, the rate of fetal loss in the Nigeria over the last 40 years has not shown a significant reduction (Gribbin and James, 2014). Most importantly, it has been reported that the majority of stillbirths have happened in the low-risk group (Gribbin and James, 20014). Thus, when fetal surveillance is performed, there might be some unidentified factors that result in the wrong identification of fetal risk and, consequently, in the incorrect assignment of some women to the low-risk group (Gribbin and James 20014). This poor outcome could be associated to human error, lack of a complete understanding of how the fetal responds to prolonged hypoxemia or perhaps lack of sensitivity in the screening tools currently available (Menihan and Kopel 2008). In any case, it is clear that there is a need of methods that effectively identify fetuses at risk in apparently low-risk pregnancies (Gribbin and James 2014).

In an attempt to increase the screening efficiency, it has been taken into account that a normally oxygenated fetal can become abnormally hypoxic (i.e. at risk) at any time during pregnancy. Consequently, attention has been paid to long-term monitoring of fetal responses to increase the possibilities of detecting dangerous hypoxic events as soon as they appear. Clearly, since long exposure to ultrasound might harm the fetal, this screening tool becomes an unsuitable option for long-term monitoring and fetal distress prediction (Barnett, 2011). Alternatively, there has been continuing development of existing technologies as well as research into new non-invasive methods that aim to improve antenatal monitoring procedures.

Until recently the approach has been the effective use of computers and human resources. Today both cultural and procedural changes are needed to support the medical profession of the future, and these changes will require Expert Software Systems involving Object-relational database System and deductive Databases (rules and facts). In this thesis, the needs for the design, implementation, and application of a Computer Software which can mimic human thought, understand logic, and handle the range of problems, which are coextensive with the range of problems to which the human mind has been applied to the topic discussed, is examined, with the objective of solving the problems of complications primarily due to both low-birth weight and excessive fetal weight at delivery usually associated with an increased risk of newborn complications during labour.

Combining the different methods of fetal weight prediction to improve their overall accuracy may be possible. By combining the independent information about fetal size obtained from the three different approaches (i.e., clinical
examination, quantitative assessment of maternal characteristics, ultrasonographic fetal biometry), the predictive value of fetal weight estimations can be improved dramatically (Dellicour, 2010).

Therefore, this paper provides computerized clinical expert system and provides solutions to these problems accompanying accuracy, effectiveness and efficiency in fetal parameters estimation.

2. Clinical Prediction Models

A clinical prediction model (CPM) is a tool for predicting healthcare outcomes, usually within a specific population and context. A common approach is to develop a new CPM for each population and context; however, this wastes potentially useful historical information. A better approach is to update or incorporate the existing CPMs already developed for use in similar contexts or populations.

Clinical prediction models (CPMs) are tools for predicting the natural course of diseases or the responses of patients to healthcare interventions, with regard to specific endpoints and observable characteristics (Steyerberg, 2017). For example, clinicians, healthcare managers and patients may be interested in assessing the risk of dying within 30 days of undergoing a heart bypass operation. We expect this risk to depend both on the characteristics of the patient, such as gender, age, and on the characteristics of the intervention, such as the experience of the surgeon. A CPM is usually developed by fitting a statistical model to existing data. The choice of model to be fitted depends on the nature of the endpoint; common choices are logistic regression (for a binary endpoint) and survival models (for a time-to-event endpoint).

CPMs have three main practical uses. First, they may be used at an individual patient level to communicate risk and aid in the decision-making process by stratifying patients into different treatment option groups (Hingorani, 2016) or to determine whether further testing is warranted to reach an appropriate decision (Steyerberg, 2010). Second, they may be used for planning healthcare services by predicting disease prevalence and future demand on services, or to explore the consequences of different local policy options. Third, they may be used in the quality management of healthcare services, where clinical audit processes compare observed with expected outcomes, given appropriate adjustments for differences in case-mix (e.g. ensuring the surgeon who takes on difficult cases, with a higher baseline risk, is appropriately compared with his/her peers who operate on lower risk patients).

In practice, CPMs are usually selected or developed for a given population and endpoint of interest. There are two general approaches: 1) develop a new CPM in the population of interest; or 2) use an existing CPM that has been developed and used in related contexts. The first approach wastes prior information, risks over-fitting, and ultimately leads to many CPMs existing for the same endpoint, which is confusing and makes it difficult to decide which one to apply in practice. The second approach may result in a CPM that is not fit for purpose, poorly calibrated and lacking discrimination. A better way forward may be to combine these approaches and work from the ‘middle ground’ in which existing CPMs that may be relevant for the population and endpoint of interest are taken, and revised to suit the new population.

Another common pitfall with CPMs is that their performance can deteriorate over time. This can be attributed to changes over time in: prevailing disease risks (e.g. the obesity epidemic accelerating the force of diabetes morbidity); unmeasured risk factors for disease and treatment outcomes; treatments; treatment settings; adjunct treatments and wider healthcare; and data quality. Therefore, to remain valid, CPMs must evolve over time – either by renewing or updating the model at discrete timepoints12, or by allowing the CPM to operate dynamically, updating continuously in an online fashion (Hickey, 2013).

The quantitative performance of a CPM can be evaluated through its discrimination (how well patients with poor outcomes are separated from those with better outcomes) and calibration (agreement between probabilities from the CPM and observed outcome proportions). These can be assessed internally (using, for example, cross-validation to correct for within-sample optimism) or, more preferably, externally using a different population. The discrimination is measured by the area under the receiver operating characteristic (ROC). The ROC is a plot of the sensitivity versus specificity for a CPM, based on dichotomizing the predicted probabilities from this CPM into disease and non-disease two groups over a continuous range of thresholds.

Focusing on the statistical literature, we have identified three main approaches for updating CPMs in light of new data. The first approach, which we term regression coefficients updating, focuses on updating some or all coefficients from an existing CPM. The second approach is meta-model updating, which synchronizes multiple existing CPMs into one new
meta-CPM. The third approach is dynamic updating, in which one or multiple CPMs can be continuously and simultaneously updated in calendar time, constantly learning from new data.

Throughout this section we consider a situation in which we have $M$ previous logistic regression models available to predict a binary outcome $Y$. These $M$ models have been developed in previous data. For model $m$, let $X_m$ denoting the design matrix of the covariates; $a_m$ and $b_m$ be the original model intercept and a vector of slopes respectively, and $LP_m$ stands for linear predictors, so the model is specified by:

$$\log \left( P(Y=1) \right) = a_m + \beta_m X_m + am + LP_m, \text{ and } m=1, \ldots, M.$$  We wish to update, potentially combine, and apply these models in new data, termed the updating dataset.

### 3. Review of Models for Estimation of Gestational age

Ultrasound assessment of gestational age up to 24 weeks provides the most accurate prediction of expected date of delivery and is more reliable than last menstrual period (Verburg et al., 2008). Although accurate gestational age assessment is not a problem unique to rural areas, there is lower availability of ultrasound dating for women in the rural area (Rijken et al., 2009). Due to the sheer numbers of births and economics in developing countries the last menstrual period remains the most widespread predictor of gestational age. In some cultures, particularly where literacy levels are low, last menstrual period can be very unreliable (Rijken et al., 2009). In such settings methods to date such pregnancies have relied on inexpensive tools including validated scored assessments of superficial and neurological newborn criteria. Training and ongoing quality control of testers is needed to maintain the accuracy of these methods. The symphysis pubis fundal height (SFH) measurement is also widely available, routinely practiced in nearly all antenatal settings in the world and simple to perform. While Neilson’s Cochrane review concludes that there is not enough evidence to evaluate the use of SFH during antenatal care, it may be the only data collected and reported in an antenatal card, in much of the resource poor world, that provides a clue to the gestation of pregnancy (Neilson, 2010). In the past 20 years SFH has taken a back seat to ultrasound in terms of gestating pregnancies but in urban areas and rural areas use SFH in routine practice as a low technology method for monitoring of fetal growth and identifying intrauterine growth restriction.

In one UK based study an obstetrician blinded to the LMP overestimated gestation by 6 weeks when assuming SFH at the umbilicus was equivalent to 20 weeks (Jimenez et al., 2013). SFH has been used as a proxy for gestational age in Africa (Andersson, 2011) and racial differences in SFH growth rates have also been documented. Crosby et al. and Engstrom et al. emphasize the considerable inter and intra observer error in their study of SFH measurements (Engstrom et al., 2012). The shape of the SFH curve with gestation has been plotted by various groups who established population curves again in the interests of being able to detect growth restriction. Two of these groups describe the use of polynomial regression as the best method to fit the SFH data (Engstrom, 2012). Few studies have modeled SFH to predict gestational age at birth (Andersson, 2011).

In refugee camps and migrant antenatal clinics on the Thai Burmese border the majority of women are unable to provide a reliable date of the last menstrual period (Rijken et al., 2009). In previous publications on malaria in pregnancy from the same area, a formula for predicting gestational age using SFH in these women was used and was found to predict gestational age with an accuracy of ±6.26 weeks.

Variations in fetal size at a given gestation can be converted into differences in gestational age. This applies just as well to ultrasound estimates (current gold standard) though this is rarely discussed (Henriksen et al., 2015). Henriksen and colleagues explored this in detail in relation to good quality history of LMP and an early ultrasound measurement of early biparietal diameter (BPD) in 3,606 women. They report that factors that reduce fetal size e.g. female sex of babies and maternal smoking, can distort the relative risk of preterm or post term delivery by 10-20% when gestational age is based on late ultrasound not LMP. Despite highly accurate fetal measurements at present, an inherent error remains in any prediction of gestational age. This manuscript refines the estimation of gestational age from SFH in women using early ultrasound derived gestation as a gold standard. Three models (formulae) were developed and compared for accuracy of predictive power. The aim of modelling SFH in this particular population was to ascertain the most reliable method of gestating pregnancies when no other reliable measure of gestation was available.

Three models were considered for the prediction of gestational age using SFH measurement. The first was a linear formula using a single SFH measure, the second was a non-linear formula using a single SFH measure and the third was a formula that used multiple measures of SFH combined with the dates of each measurement.
4. Model One: Linear formula using a single SFH measure

This model requires only a single measure of SFH and uses linear regression to model the gestational age. This is the standard linear formula (Neilson, 2010) based on a linear relationship between Dubowitz gestational age assessment (Dubowitz et al., 2000) and SFH measurements (n=100 women with normal pregnancies).

\[ G = (a_1H + a_2) \]

where \( G \) is the expected gestational age in weeks determined by ultrasound at the date of the SFH measurement and \( H \) is the SFH in cm with two estimated parameters \( a_i \). This model was transformed to a multiple measure model by, for each mother, taking the mean of the gestational age at birth predictions from each of her SFH measures.

4.1. Model Two: Non-Linear formula using a single SFH measure

Model two is a non-linear formula for predicting gestational age. A non-linear formula was considered because when SFH is plotted against gestational age at time of measurement for each mother growth appears to be initially linear followed by a plateau. A functional form was chosen that would allow such a shape while limiting the number of parameters to be estimated to only 3.

\[ G = -\left(\frac{\ln(\ln(\frac{b_1}{H}))}{b_2}\right) + b_3 \]

where \( G \) is the gestational age in weeks and \( H \) is the SFH in cm with three estimated parameters \( b_i \). This model was transformed to a multiple measure model by, for each mother, taking the mean of the gestational age at birth predictions from each of her SFH measures.

5. Summary of Achievement

The medical predictive system for comparative analysis of foetal parameters was designed to predict the Gestation Age System and illustrated how it used as a support tool for the estimation of Gestation Age. We have shown how it provides metrics for later use in growth and health evaluation modules. We have also indicated how it gives clinicians the ability to incorporate accuracy levels for the gestation age estimate and to update the actual age estimate. The new system allows the patients to access their antenatal visit records from any point of internet access point. The predictive system can also help expectant mothers to calculate the EDD on their own. The predictive system has facilities for:

- Online antenatal registration by pregnant mothers
- Online monitoring of antenatal clinic visits by pregnant mothers
- Prediction of foetal parameters using expert tool
- Monitoring of the level of antenatal participation / awareness in selected states
- Comparative analysis of the predicted EDD and the actual delivery date of the baby

6. Conclusion

This thesis have attempted to discuss a particular possibility of an ES to solve problems of complications primarily due to low and excessive birth weights at delivery by accurately estimating foetal parameters (Foetal Weight, Foetal Age Conception Date, And Delivery Date) using UltrasoundFoetal Biometric Data. The primary goal of expert system research is to make expertise available to decision makers and technicians who need answers quickly. There is never enough expertise to go around - certainly it is not always available at the right place and the right time. But computers loaded with in-depth knowledge of specific subjects can bring decades worth of knowledge and solution to a problem. If we must investigate and solve those ultrasoundfoetal biometry method of estimation that has been described over the decades as complicated, labour -intensive, limited by suboptimal visualization of foetal structures, costly and
specially requiring trained personnel, we will have to build into the estimation the use of a Computer Wizard (An Expert System).

The perception of the clinician as the final arbiter and a system’s ability for clinician override has been described as crucial in clinical decision support system integration. The issues relating to the requirements for clinician control indicate that close co-operation with medical staff is crucial in the development of our system to ensure that it can be successfully implemented. Full disclosure of the assumptions involved in the design of the system is also vital. Once again this requires a close relationship between the knowledge engineer and the expert medical staff during development to ensure that clinical guidelines are understood and are being implemented correctly.

Compliance with ethical standards

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We the authors of this manuscripts agreed that there will be no conflict of interest

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